DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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December 18, 2014

Vitrolife Sweden AB
% Anthony T. Pavel
Regulatory Counsel
Morgan, Lewis & Bockius LLP
1111 Pennsylvania Avenue NW
Washington, DC 20004

Re: K140207
Trade/Device Name: Rapid-i™ Kit
Regulation Number: 21 CFR 884.6160
Regulation Name: Assisted reproduction labware
Regulatory Class: II
Product Code: MQK
Dated: November 24, 2014
Received: November 25, 2014

Dear Anthony T. Pavel,

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-

related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Herbert P. Lerner -S

for

Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K140207

Device Name
Rapid-i™ Kit

Indications for Use *(Describe)*
The Rapid-i™ Kit is a cryopreservation device designed to contain, vitrify and maintain 4-8 cell and blastocyst stage human embryos.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

510(k) Summary

Submitted by:	Vitrolife Sweden AB Box 9080 SE-400 92 Göteborg SWEDEN	
Date:	December 16, 2014	
Manufacturing Sites:	Vitrolife Sweden AB Box 9080 SE-400 92 Göteborg SWEDEN	Vitrolife Inc. 3601 Inca Street Englewood, CO 80110 USA
Contact Person:	Nina Arvidsson Regulatory Affairs Manager Vitrolife Sweden AB Box 9080 SE-400 92 Göteborg SWEDEN Tel: +46 31 721 80 77 Fax: +46 31 721 80 90 E-mail: narvidsson@vitrolife.com	
Establishment Registration Numbers:	3003995932 Vitrolife Sweden AB	9037178 Vitrolife Inc., Englewood, CO
Device Trade Name:	Rapid-i™ Kit	
510(k) Number:	K140207	
Device Common Name:	Cryopreservation container and microtool	
Device Classification:	Regulation: 21 C.F.R. § 884.6160 Classification Name: Assisted Reproduction Labware Product Code: MQK Classification: Class II (special controls)	
Device Classification:	Class II	

Predicate Device: Vitrolife Rapid-i™ (K090832)

Indications for Use: The Rapid-i™ Kit is a cryopreservation device designed to contain, vitrify and maintain 4-8 cell and blastocyst stage human embryos.

Device Description and Principles of Operation: Rapid-i™ Kit, a cryopreservation device designed to contain, vitrify and maintain 4-8 cell and blastocyst stage human embryos, consists of the following three items:

- 80 mm PMMA stick (Rapid-i™)
- 135 mm Mediprene straw equipped with a stainless steel weight, (RapidStraw)
- 115 mm stainless steel rod inserted in the RapidStraw

4-8 cell and blastocyst stage embryos are vitrified using the Rapid-i™ Kit by pre-cooling the RapidStraw (steel rod inserted) with the open end extending from the liquid nitrogen. A 30 nanoliter drop of vitrification solution holding embryos is placed in a capillary sized hole in the Rapid-i™. The stainless steel rod is removed 20-30 seconds before the Rapid-i™ is inserted in the pre-cooled RapidStraw in liquid nitrogen to effect vitrification of the embryos. The open end of the straw is then sealed.

Substantial Equivalence to Predicate Devices: The Rapid-i™ Kit is substantially equivalent to the Rapid-i™, as previously cleared by FDA (K090832).

The following table compares the Rapid-i™ Kit to the predicate device (Rapid-i™) with respect to intended use, technological characteristics, and principles of operation.

Manufacturer	**Vitrolife Sweden AB**	**Vitrolife Sweden AB**
Trade Name	Rapid-i™ Kit	Rapid-i™
510(k) Number	K140207	K090832
Product Code	MQK	MQK
Regulation Number	884.6160	884.6160
Regulation Name	Assisted Reproduction Labware	Assisted Reproduction Labware
Indications for Use	The Rapid-i™ Kit is a cryopreservation device designed to contain, vitrify and maintain 4-8 cell and blastocyst stage human embryos.	Rapid-i™ is a cryopreservation device that is intended to be used to contain, vitrify and maintain 4-8 cell stage embryos.

Manufacturer	Vitrolife Sweden AB	Vitrolife Sweden AB
Method of Action (vitrification)	Precool a straw with the open end extending from the liquid nitrogen. A 30 nanoliter drop of vitrification solution holding embryos is placed in a capillary sized hole in the stick. The stick in turn is inserted in the pre cooled straw in liquid nitrogen to effect vitrification of the embryos. Subsequently, the open end of the straw is sealed.	Precool a straw with the open end extending from the liquid nitrogen. A 30 nanoliter drop of vitrification solution holding embryos is placed in a capillary sized hole in the stick. The stick in turn is inserted in the pre cooled straw in liquid nitrogen to effect vitrification of the embryos. Subsequently, the open end of the straw is sealed.
Cooling Rate	1400°C/min at -50°C	1400°C/min at -50°C
Method of Action (rewarming)	While the distal end of the straw remains in liquid nitrogen, cut the sealed proximal end of the straw. Withdraw the stick and directly immerse the stick/vitrified drop in warming media.	While the distal end of the straw remains in liquid nitrogen, cut the sealed proximal end of the straw. Withdraw the stick and directly immerse the stick/vitrified drop in warming media.
Rewarming Rate	10,000°C/min at -50°C	10,000°C/min at -50°C
Warming: Contact With the Warming Medium	Direct immersion of sample in the warming solution for simultaneous thawing and dilution.	Direct immersion of sample in the warming solution for simultaneous thawing and dilution.
Materials in Contact With Tissue (embryos)	Polymethyl methacrylate (PMMA) stick with hole, 2x80 mm	Polymethyl methacrylate (PMMA) stick with hole, 2x80 mm
Straw	Mediprene straw with funnel and weight, OD 3.45 mm, ID 2.5 mm, wall thickness 0.47 mm, length 135 mm	Poly vinyl chloride (PVC) straw with funnel and weight, OD 3.3 mm, ID 2.6 mm, wall thickness 0.35 mm, and length 165 mm
Stainless Steel Rod	Stainless steel, 2.2 x 115 mm	----

Manufacturer	Vitrolife Sweden AB	Vitrolife Sweden AB
Sterility Assurance Level	Sterilized by ethylene oxide. SAL is 10^{-6}	Sterilized by ethylene oxide. SAL is 10^{-6}
MEA Specification	Mouse Embryo Assay (1 -cell) % expanded blastocyst, within 96h ≥80	Mouse Embryo Assay (1 -cell) % expanded blastocyst on day 5 ≥80
Endotoxin Specification	Bacterial endotoxins (LAL assay) <1 EU/device	Bacterial endotoxins (LAL assay) <1 EU/device

Discussion of Similarities and Differences

The indication for the cleared Rapid-i™ is "a cryopreservation device that is intended to be used to contain, vitrify and maintain 4-8 cell stage embryos." The addition of blastocyst stage embryos to the proposed device's indication does not represent a new intended use. Both the proposed and predicate devices are intended to cryopreserve embryos from patients undergoing assisted reproductive procedures for later use. Blastocyst stage embryos and 4-8 cell stage embryos are similar in size and morphology and therefore the same carrier devices may be used for the vitrification of embryos in both of these stages. Therefore, addition of blastocyst vitrification does not represent a new intended use as it does not raise different questions of safety or effectiveness.

The operation of both devices is substantially similar, as both involve the precooling of a straw with the open end extending from the liquid nitrogen. The proposed device utilizes a stainless steel rod, which acts to keep the straw straight and also helps limit condensation in the straw during the cooling procedure, and is removed prior to insertion of the Rapid-i™ stick. The inclusion of the stainless steel rod does not raise any new questions of safety or effectiveness. A 30 nanoliter drop of vitrification solution holding embryos is placed in a capillary sized hole in the stick. The stick in turn is inserted in the pre-cooled straw in liquid nitrogen to effect vitrification of the embryos. Subsequently, the open end of the straw is sealed. The warming procedures are the same for both devices, and the cooling and warming rates of the devices are the same, as are the materials in contact with the embryos.

The straw in the proposed device is comprised of mediprene (straw with funnel and weight, 3.45 x 135 mm), whereas in the predicate, the straw is comprised of polyvinyl chloride (PVC) (straw with funnel and weight, 3.3 x 165 mm).

The change in material from PVC to mediprene has no impact on function and was made because of improved color properties of the material. The difference in material does not raise any new questions of safety or effectiveness.

The RapidStraw was shortened to fit better in devices used to hold samples in

liquid nitrogen storage tanks. The straw diameter was increased to aid in insertion of the Rapid-i™ stick into the RapidStraw. Also, the wall thickness of the straw was increased. None of these changes raises new questions of safety or effectiveness.

Accordingly, Vitrolife has concluded that the technology of the proposed device is substantially equivalent to the predicate device and that differences do not raise new questions of safety or effectiveness.

Nonclinical Testing

The Rapid-i™ Kit is substantially equivalent to the previously-cleared Rapid-i™ (K090832), and is subject to the following tests:

A. Mouse Embryo Assay

Rapid-i™ Kit is subject to the 1-cell Mouse Embryo Assay (MEA).

Specification: Mouse Embryo Assay (1-cell) [% expanded blastocyst within 96 hours] ≥ 80 %.

B. Endotoxin Testing

Rapid-i™ Kit is subject to bacterial endotoxin testing by use of the LAL assay.

Specification: Bacterial Endotoxins (LAL assay) ≤ 1.0 EU/device.

Testing is performed according to USP<85> Bacterial Endotoxins Test.

C. Sterilization Validation

Sterility of the device is assured through the use of ethylene oxide sterilization.

Specification: Sterilized using ethylene oxide SAL 10^{-6}.

Sterilization validation was performed according to ISO 11737-2:2009 Sterilization of Medical devices – Microbiological Methods, Part 2: Tests of Sterility Performed in the Validation of the Sterilization Process.

D. Design Validation

As part of the design validation process, the following tests were conducted on the Rapid-i™ (K090832) (which is substantially similar to the Rapid-i™ Kit):

The design validation testing on the post-seal Rapid-i™ described below is valid for Rapid-i™ Kit as well. The minimal physical differences between the post-seal Rapid-i™ and the Rapid-i™ Kit are only in the straw material and the straw thickness. Neither of these parameters affects the embryo, as the straw is

not in direct or indirect contact with the embryo. The changes do not affect cooling or warming rates. Hence, the differences do not affect vitrification, warming, or embryo development after vitrification.

- Effects of sealing before and after vitrification- the purpose of the study was to evaluate different non-liquid nitrogen (LN2) contact vitrification methods of previously frozen day 1 embryos. The methods were: (a) post-seal Rapid-i™ (*i.e.*, the predicate device); (b) pre-seal Rapid-i™; and (c) the HSV straw. A non-vitrified group was used as control. The methods were evaluated with respect to expanded blastocyst development, cell count of expanded blastocysts on day 5, and ease of use and time in the final solution prior to vitrification. The study showed that the three methods did not differ from each other significantly in terms of expanded blastocyst development.

- A comparative mouse study- similar to the study above, the purpose was to evaluate different non-LN2 contact vitrification methods of fresh F1 mouse embryos. The methods were: (a) post-seal Rapid-i™ (*i.e.*, the predicate device); (b) pre-seal Rapid-i™; and (c) the HSV straw. A non-vitrified group was used as control. The methods were evaluated with respect to blastocyst development on day 4 and 5 and cell count of expanded blastocysts on day 5. The study showed that the three methods did not differ from each other significantly in terms of blastocyst development on day 4 and 5.

- A comparative Swiss outbred study- similar to the studies above, the purpose was to evaluate different non-LN2 contact vitrification methods of Swiss outbred mice. The methods were: (a) post-seal Rapid-i™ (*i.e.*, the predicate device); and (b) pre-seal Rapid-i™. A non-vitrified group was used as control. The methods were evaluated with respect to blastocyst development on day 4 and 5 and cell count of expanded blastocysts on day 5. The study showed that method (a) showed a significantly higher blastocyst development rate on day 5 and cell count of expanded blastocysts compared to method (b).

- A vitrification study- the purpose of the study was to visually verify that the post-seal Rapid-i™ and pre-seal Rapid-i™ vitrification methods result in total vitrification of the media. The methods were: (a) post-seal Rapid-i™ (*i.e.*, the predicate device) loaded with the final vitrification media; (b) pre-seal Rapid-i™ loaded with the final vitrification media; and (c) pre-seal Rapid-i™ loaded with the an intermediate vitrification media with lower osmolality. No embryo was used. The methods were evaluated by capturing images of the media in the device under LN2. The study showed that methods (a) and (b) resulted in transparent media indicating that vitrification had taken place and method (c) resulted in opaque media indicating that freezing had occurred.

E. Shelf-life Evaluation

The initial shelf-life report provided in the prior submission (K090832) for the Rapid-i™ device was based on sterile integrity of the packaging. A verifying stability study was also performed on the Rapid-i™ device. The testing included sterility testing according to USP<71> Sterility Tests, bacterial endotoxins according to USP<85> Bacterial Endotoxins Test, and Mouse Embryo Assay.

The data provided supports the proposed shelf-life for the updated version of the device because:

- Sterility Testing (Negative, no growth): sterile integrity is dependent on the primary packaging and the sealing procedure. This has not changed from the predicate.
- Endotoxin (≤1.0 EU/device): endotoxins do not change during the shelf life if packaging maintains a sterile barrier. This has not changed from the predicate.

Mouse Embryo Assay (re-expanded blastocyst within 96 hours ≥80%) has been performed on three individually tested samples from each of three lots of the proposed device. All devices met acceptance specifications, and support the 22 month shelf-life of the device.

F. Cooling/Warming Rate Testing

Cooling and warming rate testing was conducted on the predicate device (K090832). New testing is not required for the current submission for the following reasons:

- The design of the Rapid-i™ stick has not changed. Therefore, this component does not raise any new design features that may impact cooling/warming rates.
- The RapidStraw material and dimensions have been modified in comparison to the predicate device (see Substantial Equivalence to Predicate Devices section above). These changes to the straw do not impact the cooling rate of the device for the following reasons (Note: the Rapid-i™ stick is removed from the RapidStraw prior to warming, and does not impact device warming rates):
    - The RapidStraw is placed in an infinite heat sink (liquid nitrogen bath) which assures that the temperature of the inside of the RapidStraw is very close in thermal balance with the surrounding liquid nitrogen prior to loading the Rapid-i™ stick. Changes in wall thickness and use of a comparable material support comparable cooling rates when using this pre-cooling procedure.
    - Dimensional changes resulted in a decrease of 0.1 mm in the internal diameter of the RapidStraw. Therefore, the amount of space containing air between inner RapidStraw wall and the

vitrification solution has decreased by 0.05 mm, which would have an insignificant impact on cooling rates when using the pre-cooling method described above.

G. Dimension Testing

The dimensions of the finished product were measured to confirm conformance to the specifications.

Clinical Testing

The indication was modified to expand use with blastocyst stage embryos, and additional testing was performed to assess the ability to vitrify blastocyst stage embryos using the device, as discussed below.

All laboratory procedures including embryo assessment were performed according to standard procedures. For vitrification and warming, respectively, Vitrolife's RapidVit Blast and RapidWarm Blast solutions were used while the Rapid-i™ Kit was used as a carrier device. During the vitrification and warming procedures, the instructions for use for the respective procedures were followed. After vitrification, blastocysts were stored in liquid nitrogen until the time of warming. After warming, cultured and surviving embryos were transferred into the uterus using standard procedures.

The use of the Rapid-i™ Kit as carrier device for clinical blastocyst vitrification provides good results. The clinical pregnancy rates range between 32% and 47%, and to date, birth of 124 children. Clinical blastocyst vitrification was conducted at four sites, including 426 patients with embryo transfer. The average blastocyst survival rate was 91% and the average clinical pregnancy rate was 42%.

When compared with the most recent Assisted Reproductive Technology ("ART") National Summary Report, published by the Centers for Disease Control and Prevention ("CDC"), the success rates with the Rapid-i™ Kit are comparable to the 2011 ART success rates. For example, in 2011, CDC reported a mean of 36.6% of frozen embryos from nondonor eggs transferred (all ages combined) resulted in pregnancy. By comparison, the clinical pregnancy rates for the Rapid-i™ Kit ranged between 32% and 47%.

Conclusion

The nonclinical and clinical testing described above demonstrate that the Rapid-i™ Kit is substantially equivalent to the predicate device.